American Journal of Medical Genetics 62:230–232 (1996)

Mental Retardation, Epilepsy, Short Stature, and Skeletal Dysplasia: Confirmation of the Gurrieri Syndrome

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We report on a male with severe mental retardation, epilepsy, short stature, and skeletal dysplasia. The syndrome was first delineated by Gurrieri et al. in 1992 [Am J Med Genet 44:315–320]. This case seems to confirm the existence of the Gurrieri syndrome.

KEY WORDS: mental retardation, epilepsy, multiple congenital anomalies, skeletal dysplasia, Gurrieri syndrome, autosomal recessive inheritance

INTRODUCTION

Recently, Gurrieri et al. [1992] reported on four Italian sibs with a previously undescribed constellation of manifestations. The patients had moderate to severe mental retardation, seizures, short stature, and skeletal abnormalities. We report on another Italian patient with similar manifestations.

CLINICAL REPORT

The patient (F.G.), 14½ years old (Figs. 1, 2), was born at term to unrelated parents after an uneventful pregnancy, by normal delivery. The father and the mother were 22 and 18 years old, respectively. Birth weight was 2,900 g, length was 49 cm, occipito-frontal circumference (OFC) was 34 cm, and the infant was in good condition.

Psychomotor development was delayed; the boy sat unsupported by 14 months and walked with hands held by 3 years and alone by 6 years. Sphincter control was never achieved. At 2 years 7 months he developed seizures characterized by tonic-clonic movements involving all four limbs, with diffuse "epileptiform activity" on the electroencephalogram. A brain CT scan showed moderate enlargement of subarachnoid spaces. Atypical absences were noted at 4 years, followed by several other epileptic episodes, in spite of appropriate antiepileptic therapy. At the same age X-ray studies showed a retarded bone age.

When examined by us, at age 14½ years, he had severe psychomotor retardation; language was absent; social interaction was very poor; and his comprehension of spoken language was limited to very simple contextual orders. He had a stooped posture and could walk with flexed hips and knees and a festinating gait. He had a generalized symptomatic epilepsy and was receiving valproate and nitrazepam. The EEG showed a slow background activity, mixed with some spikes, particularly over the posterior half of the head, rhythmic components slower than usual, and diffuse bursts of irregular slow waves, particularly over both fronto-central areas. On physical examination OFC was 52 cm (−2 SD), height was 153 cm (3rd centile),and weight was 43.5 kg (10th centile). He was brachycephalic; had a prominent nasal root, with a short, hypoplastic philtrum; mid-face hypoplasia; half-open mouth with dental malocclusion; and wide palate. The hands were long, with camptodactyly of the 5th finger. The palmar creases were regular and shallow. Dermatoglyphics were on right: *t, a b,* Lu W W W W, and on left: *t, a b c,* W p Lr W W Lu.

The toes were long and regular. There were cervical hyperlordosis, dorsal kyphosis, pectus carinatum, lumbar scoliosis, hyperextensibility of wrists and fingers, genua valga, and flat feet with distal limb muscles hypotrophy. The skin was smooth with visible subcutaneous venous reticulation. Genitalia were normal male, though underdeveloped for the age. Results of abdominal and heart ultrasonography were normal. Urinary mucopolysaccharides, chromatography of aminoacids and oligosaccharides in plasma and urine, determination of aryl-sulfatase A, β-glucuronidase, β-hexosaminidase A and B, β-galactosidase, α-fucosidase, and α-mannosidase were within the normal range. Results of other laboratory investigations including chromosome analysis, blood lactic and pyruvic acid, thyroid and adrenal functions, and HGH after GRH stimulation, were all normal. Brain MRI showed moderate enlargement of periencephalic liquoral spaces of the frontal convexity. Ocular examination documented bilateral keratoconus.

Received for publication May 17, 1995; revision received October 30,1995.

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Fig. 1. Patient at 14 years.

Fig. 2. Close-up view of the patient.

Skeletal X-ray studies showed accentuation of the dorsal kyphosis, schisis of S1, hypoplasia of iliac alae, hypoplastic acetabula, anomalous bilateral apophisis on the inferior iliac margin of the sacro-iliac synchondrosis, two tubercles on the superior and inferior profile of the right obturator foramen (Fig. 3), and decreased anterio-posterior diameter of L2–L5 (Fig. 4). Electromyography was normal.

Fig. 3. Pelvic X-ray film of the patient. Note hypoplasia of iliac alae and acetabula, anomalous apophisis more obvious on the left sacro-iliac synchondrosis, and two tubercles on the right obturator foramen.

Fig. 4. Spine of the patient. Note decreased antero-posterior diameter of L2–L5.

DISCUSSION

Our patient's manifestations seem to be identical to those of the cases reported by Gurrieri et al. [1992] (Table I). Skeletal dysplasia is associated with moderate to severe mental retardation, epilepsy, cerebral atrophy and eye abnormalities.

Our case has severe mental retardation with absence of speech; his central nervous system anomalies were limited to a moderate enlargement of periencephalic liquoral spaces of the frontal convexity, thus confirming the variability of such findings in this MCA/MR syndrome. The clinical and electroencephalographic aspects of the seizures are consistent with a symptomatic generalized epilepsy, of rather early onset. However, our patient never had infantile spasms. The bilateral keratoconus also present in our case confirms the occurrence and type of eye involvement in this syndrome.

The short stature, probably of postnatal onset, is associated with hypoplastic iliac alae, hypoplastic acetabula, decreased anterio-posterior diameter of lumbar vertebral bodies, retarded bone age, and some other minor skeletal abnormalities. These latter, not found in the cases of Gurrieri et al. underline the variability of manifestations in this condition, whose mode of inheritance appears to be autosomal recessive.

TABLE I. Main Clinical Findings of the Syndrome

Clinical finding	Gurrieri et al. [1992] (n = 4)	Our case
Low birthweight	4/4	+
Short stature	4/4	+
Deep-set eyes	3/4	±
Short philtrum	4/4	+
Dorsal kyphosis	4/4	+
Joint laxity	4/4	+
Hypotonia	4/4	+
Mental retardation	4/4	+
Seizures	4/4	+
EEG abnormalities	4/4	+
Abnormal brain CT scan/MRI	3/4	+
Eye abnormalities	4/4	+
Abnormal X-ray of pelvis and spine	4/4	+
Retarded bone age	2/4	+

ACKNOWLEDGMENTS

We thank Prof. G. Neri of the Istituto di Genetica Medica, Facoltà di Medicina A. Gemelli, Roma for his collaboration with the analysis of dermatoglyphics of our patient.

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